REMARKS

Claims 9 and 13-20 presently appear in this case. No claims have been allowed. The official action of July 22, 2004, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly the present invention relates to novel isolated polypeptides that are involved in the process of apoptosis, as well as analogs and derivatives thereof and antibodies thereto.

Claims 9 and 13-15 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The examiner states that in claim 13(a)(iii), there is insufficient antecedent basis, but that this would be cured by amending the claim to recite the phrase "the protein encoded by the full length cDNA."

Claim 13 has now been amended as suggested by the examiner, thus obviating this part of the rejection.

Claims 14 and 15 are considered indefinite because of the phrase "polypeptide in accordance with claim 13."

While applicant believes that this rejection is totally absurd, as there are tens of thousands of patents that use this common language, which language has been used throughout the thirty year career of the undersigned,

nevertheless, to obviate the rejection, the claims have been amended as suggested by the examiner.

Claims 9 and 13-17 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The examiner states that, while the specification discloses that the expression of mRNA is elevated in cells treated with hypoxic conditions, the specification is silent on whether the protein encoded by said mRNA is also elevated significantly, or even expressed at all at a cellular level. The examiner states that, absent evidence that the protein of SEQ ID NO:4, which is encoded by the polynucleotide of SEQ ID NO:3, is actually present in cellular levels, and that said protein is differentially overexpressed in cells subject to hypoxic conditions, one skilled in the would not be able to practice the invention as claimed without undue experimentation. This part of the rejection is respectfully traversed.

Attached hereto is a declaration of Dr. Peter Chumakov, which reports a number of experiments that were performed under his direction and control. Using antibodies against the protein, he was able to determine that elevated expression of the gene 95 polypeptide was detected following treatment of cells with H_2O_2. Furthermore, induction of gene 95 polypeptide expression was completely abolished in RKO

cells in which p53 expression was inactivated via RNA interference, while in contrast, both types of cells retained the ability to strongly induce the gene 95 polypeptide in response to H_2O_2. Thus, this declaration clearly establishes that, in addition to elevation of gene 95 mRNA levels, the expression of the gene 95 polypeptide is indeed induced in humans in response to oxidative stress, thus confirming the statements made in the present specification. In light of this evidence, reconsideration and withdrawal of this part of the rejection is respectfully urged.

The examiner states that the specification further lacks evidence on whether the sequence variants within the scope of the claim are present at the cellular level, and whether they are overexpressed in cells subjected to hypoxic conditions. This part of the rejection is also respectfully traversed.

Claim 13(a)(ii) is directed to a protein encoded by a strand of a full length cDNA having the sequence of a naturally occurring polynucleotide, having at least 85% identity with SEQ ID NO:3, and having certain properties. It has already been established by the Chumakov declaration discussed above that the protein encoded by a strand of a full length cDNA having a sequence comprising the sequence of SEQ ID NO:3 does indeed have utility, and one would be able to

practice the invention as claimed without undue experimentation. Given that, and given the fact that claim 9 has now been amended to require at least 85% identity in section (a)(ii) (as is supported by the present specification at page 18, paragraph 53), it is not incredible to believe that naturally occurring cDNAs of such related sequences would operate in the same way, particularly as the claim requires that they do so in order to fall within the scope of the claim. This language covers allelic variations, as it always requires that the cDNA be naturally occurring. Once one isolates such a naturally occurring full length cDNA, which has at least 85% identity to SEQ ID NO:3, it would not take undue experimentation to determine whether or not the expression of the protein encoded thereby is modulated when the cells are subjected to neurotoxic stress, and that that protein induces cell apoptosis when overexpressed in human epithelial breast carcinoma NCF7 cells.

Similarly, section (a)(iii) of claim 13 has now been amended to specify that the hybridization is conducted under highly stringent conditions, which is consistent with the 85% identity in section (a)(ii). Accordingly, the enablement requirement is fulfilled with respect to this definition as well.

With respect to paragraph (b) of claim 13, this has now been amended to specify that the variant has at least 90% identity to the protein of (a) (see page 26, paragraph 71), and new claims 18, 20 and 22 specify that they have at least 95% identity. Because of the very high degree of identity and the relatively small number of changes that this encompasses, it would not take undue experimentation to make random mutations and test to see whether such protein induces cell apoptosis when overexpressed in human epithelial breast carcinoma MCF7 cells, which assay is fully described in the present specification.

Accordingly, in view of the amendments to the claims and the attached Chumakov declaration, it is urged that all of the present claims now fully comply with the enablement requirement of 35 U.S.C. §112. Reconsideration and withdrawal of this rejection is therefore respectfully urged.

Claims 9 and 13-15 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The examiner states that the specification provides insufficient written description to support the genus encompassed by the claim, which permits variance of as low as 70% identity. This rejection is respectfully traversed.

The examiner's attention is invited to the Synopsis of Application of Written Description Guidelines, and particularly Example 14 thereof. There, the Patent and Trademark Office analyzed a claim reading:

> A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3, and catalyzed the reaction of A->B.

The analysis under the written description guidelines concluded that even though this claim was supported only by the single example of SEQ ID NO:3, it satisfied the written description requirement, because the single species disclosed is representative of the genus, because all members that have at least 95% structural identity with the reference compound, and because of the presence of an assay, which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3, which are capable of the specified catalytic activity. Thus, one of ordinary skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus. This example advises examiners that in such a case, the disclosure should be held to meet the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Claims 18, 20 and 22 specify variants with at least 95% identity. The written description rejection should be

withdrawn with respect to these claims. Similarly, with respect to the claim stating a variant of 90% identity, there is no reason why this should not be considered similarly to the manner in which the Office considers 95% identity under the written description guidelines. 95% was merely an example, and there is no reason to believe that 90% identity would not also be considered to fulfill the written description requirement. An activity and an assay are set forth in the present specification.

Similarly, with respect to the identity for the naturally occurring cDNAs, while the degree of variance is slightly broader in reciting 85%, or that which hybridizes under highly stringent conditions, it is a smaller class of species, as there are only a relatively small number of naturally occurring polynucleotides that will have the specified properties. Thus, it should be considered to satisfy the written description requirement for the same reason as discussed above in light of Example 14 of the synopsis.

The examiner's attention is also invited to Example 9 of the same Synopsis of Application of Written Description Guidelines, which analyze the claim that reads:

> An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the compliment of the sequence set forth in SEQ ID NO:1, wherein said nucleic acid

encodes a protein that binds to a dopamine receptor and stimulates adenalate cyclase activity.

That analysis led to the conclusion that the claimed invention was adequately described, even though only a single species was disclosed that was within the scope of the claimed genus. For this reason as well, the language of claim 13 as a whole should be considered to satisfy the written description requirement of 35 U.S.C. §112. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

It is submitted that all of the claims now present in this case clearly define over the references of record and fully comply with 35 U.S.C. §112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this amendment with declaration and PTO-2038 (credit card payment form) is being facsimile transmitted to the Patent and Trademark Office, on the date shown below.

Jonathan Brammer
Name

Signature

January 21, 2005
Date